UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,882	06/14/2005	Syunichirou Oshima	273243US0PCT	8838

22850 7590 01/04/2008

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
01/04/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/538,882	OSHIMA ET AL.	
	Examiner	Art Unit	
	Lakia J. Tongue	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on October 4, 2007 is acknowledged. Claims 1-3 and 5-24 are pending. Claims 1, 2 and 12-14 have been amended. Claims 4 and 25-30 have been canceled. Claims 1-3 and 5-24 are under consideration.

Rejections Withdrawn

1. In view of Applicant's amendment the rejection of claims 1-3 and 5-24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. The cancellation of claims 4 and 25-30 renders the rejection of said claims moot. The amendment to claims 1, 2, 12, and 13 to recite "cultivated from a logarithmic growth phase culture" obviates said rejection. The amendment to claim 14 to recite "wherein said components of inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture are obtained from cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture that have been inactivated by formalin treatment" obviates this rejection.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. The rejection of claims 1-3, 5-9, 12-16, 20-22 and 24 under 35 U.S.C. 102(a) as being anticipated by LaFrentz et al. (Journal of Fish Disease, 2002; 25: 703-13) is maintained for the reasons set forth in the previous office action. The cancellation of claims 4 and 26-30 renders the rejection of said claims moot.

Applicant argues that:

1) LaFrentz et al. does not disclose inactivation of a logarithmic growth phase culture.

2) There is no disclosure in the reference to show such an increase in cell number during their growth conditions.

3) Applicants submit that the culture would not be in logarithmic phase as the Examiner alleges, but rather they would be in the stationary phase, which is further evidenced by an executed Declaration under 37 C.F.R. §1.132 evidencing that the cultures in the art of record are, in fact, "stationary phase".

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to a pharmaceutically administrable composition comprising inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture and at least one pharmaceutically acceptable carrier or adjuvant. Subsequent claims are drawn to a method for preventing the cold-water

disease in fish, comprising administering an effective dosage of said composition to a fish in need thereof to prevent cold-water disease.

With regard to Points 1 and 2, contrary to Applicant's response the culture conditions of LaFrentz et al. are such that the cells would be in logarithmic phase. This is evidenced by LaFrentz et al. where it is disclosed that *F. psychrophilum* cultures were grown in 2 L volumes for 72 hours (see pages 704-705). In absence of evidence to the contrary the cultures would be in logarithmic phase.

With regard to Point 3, the Declaration under 37 C.F.R. §1.132 submitted on October 4, 2007 by Shun-Ichirou Oshima has been fully considered and deemed non-persuasive. The data disclosed in the declaration is not commensurate in scope with the data presented in LaFrentz et al. The deceleration discloses differing compositions, which comprise various medias. Moreover, the data presented in the declaration does not use the exact parameters as that which was disclosed in the reference (see number 5 of the declaration). This is evidenced by Applicants submission that they started culturing with commonly used conditions, namely used cells from frozen stock of about 10^9 CFU/ml. This is further evidenced by the statement "proliferating potential of bacteria in each culture can be expected to be at the similar level since the culture conditions are quite similar to each other", indicating that while the cultures are similar they are not one in the same.

As previously presented, LaFrentz et al. disclose a vaccine that comprises killed *Flavobacterium psychrophilum* cells, which were effective against bacterial coldwater disease in fish (page 705 &710; 1st column). LaFrentz et al. disclose that

Flavobacterium psychrophilum cells were killed by formalin and harvested by centrifugation. Moreover, LaFrentz disclose that the cells were re-suspended in physiological saline (page 705, 1st column, 1st paragraph). Inherently, the inactivated cells components comprise cell membrane components, vesicles, and/or secretary products.

It should be remembered that the products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same or similar functional characteristics, i.e. the ability to prevent cold water disease in fish. The purification, isolation or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the process (i.e. isolation via centrifugation, filtration, or ultrasonic pulverization) does not change properties of the product in an unexpected manner. See *In re* Thorpe, 227 USPTO 964 (CAFC 1985); *In re* Marosi, 218 USPTO 289, 29222-293 (CAFC 1983); *In re* Brown, 173 USPTO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, great stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts to applicants product in order to overcome the aspect of the product's purity.

Moreover, LaFrentz et al. disclose a method for preventing cold-water disease in rainbow trout by administering a vaccine comprising killed *Flavobacterium psychrophilum* cells (pages 704- bacterial culture; 705-fish immunizations). Additionally, LaFrentz disclose that the fish were immunized by immersion. Bath solutions were prepared by suspending formalin-killed *Flavobacterium psychrophilum* cells in water. For rainbow trout immunizations, an additional immersion was included (page 705, immersion delivery). The method of the prior art is the same of that which is claimed. Limitations such as an effective dosage range and when to collect inactivated cells are being viewed as limitations of optimizing experimental parameters.

3. The rejection of claims 1-3, 5-8, 12-15, 20-22 and 24 under 35 U.S.C. 102(b) as being anticipated by Masunari et al. (Bulletin of the Fisheries Experiment Station, Okayama Prefecture, 2001; 16: 49-57 (translation pages 1-14)) is maintained for the reasons set forth in the previous office action. The cancellation of claims 4, 26-28 and 30 renders the rejection of said claims moot.

Applicant argues that:

1) Masunari et al. does not disclose inactivation of a logarithmic growth phase culture.

2) There is no disclosure in the reference to show such an increase in cell number during their growth conditions.

3) Applicants submit that the culture would not be in logarithmic phase as the Examiner alleges, but rather they would be in the stationary phase. This further

evidenced by an executed Declaration under 37 C.F.R. §1.132 evidencing that the cultures in the art of record are, in fact, "stationary phase".

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to a pharmaceutically administrable composition comprising inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture and at least one pharmaceutically acceptable carrier or adjuvant. Subsequent claims are drawn to a method for preventing the cold-water disease in fish, comprising administering an effective dosage of said composition to a fish in need thereof to thus prevent cold-water disease.

With regard to Points 1 and 2, contrary to Applicant's response the culture conditions of Masunari et al. are such that the cells would be in logarithmic phase. Masunari et al. disclose that *F. psychrophilum* were cultured in modified cytophaga broth at 18 °C for 3-3.5 days, where the number of bacteria before inactivation was 3.6 x 10^6 CFU/ml and 4.3 x 10^6 FCU/ml (see page 4; vaccine preparation). In absence of evidence to the contrary the cultures would be in logarithmic phase.

With regard to Point 3, the Declaration under 37 C.F.R. §1.132 submitted on October 4, 2007 by Shun-Ichirou Oshima has been fully considered and deemed non-persuasive. The data disclosed in the declaration is not commensurate in scope with the data presented in Masunari et al. Moreover, the data presented in the declaration does not use the exact parameters as that which was disclosed in the reference (see number 5 of the declaration). The deceleration discloses differing compositions, which comprise various medias. This is evidenced by Applicants submission that they started

culturing with commonly used conditions, namely used cells from frozen stock of about 10^9 CFU/ml. This is further evidenced by the statement "proliferating potential of bacteria in each culture can be expected to be at the similar level since the culture conditions are quite similar to each other", indicating that while the cultures are similar they are not the same.

As previous presented Masunari et al. disclose a vaccine comprising formalin-killed *Flavobacterium psychrophilum* cells. Moreover, Masunari et al. disclose that the vaccine is to be used for the prevention of the cold-water disease in Ayu (fish) (see page 4, paragraph 3; title). The vaccine of the prior art is the same of that which is claimed. Inherently, the inactivated cells components comprise cell membrane components, vesicles, and/or secretary products.

It should be remembered that the products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same or similar functional characteristics, i.e. the ability to prevent cold water disease in fish. The purification, isolation or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the process (i.e. isolation via centrifugation, filtration, or ultrasonic pulverization) does not change properties of the product in an unexpected manner. See *In re* Thorpe, 227 USPTO 964 (CAFC 1985); *In re* Marosi, 218 USPTO 289, 29222-293 (CAFC 1983); *In re* Brown, 173 USPTO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant needs to show some unexpected and unique utility or

property, such as unexpected biologically significant increase in specific activity with which the increased purity, great stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts to applicants product in order to overcome the aspect of the product's purity.

Moreover, Masunari et al. disclose a method for preventing the cold-water disease in fish, comprising administering 0.05 ml of inactivated cells of *Flavobacterium psychrophilum* to fish (see page 4, paragraph 4). The method of the prior art is the same of that which is claimed. Limitations such as an effective dosage range and when to collect inactivated cells are being viewed as limitations of optimizing experimental parameters.

4. The rejection of claims 1-3, 5-8, 12-15, 20-22 and 24 under 35 U.S.C. 102(b) as being anticipated by Rahman et al. (Fish and Shellfish Immunology, 2002; 12: 169-79) is maintained for the reasons set forth in the previous office action. The cancellation of claims 4, 26-28 and 30 renders the rejection of said claims moot.

Applicant argues that:

1) Rahman et al. does not disclose that the logarithmic growth phase cells were inactivated. Moreover, contrary to the Examiner's assertion, the OMF vaccine was not prepared by inactivation with formalin (see method disclosed on page 171, first full paragraph).

2) As shown in the Declaration, after 72 hours a culture of *F. psychrophilum* is in stationary phase, not logarithmic phase as required by the present invention.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to a pharmaceutically administrable composition comprising inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture and at least one pharmaceutically acceptable carrier or adjuvant. Subsequent claims are drawn to a method for preventing the cold-water disease in fish, comprising administering an effective dosage of said composition to a fish in need thereof to thus prevent cold-water disease.

With regard to Point 1, Rahman et al. disclose that cultures were grown and harvested by centrifugation while still in logarithmic growth phase (see page 173; culture conditions in broth medium). Further, Rahman et al. disclose that formalin killed bacteria was used for the vaccine in question (see page 170). Moreover, the abstract of Rahman et al. disclose that the present study sought to assess the efficacy of a *F. psychrophilum* vaccine based on the antigenic outer membrane fraction. The abstract goes on to disclose that the fraction induced significantly higher protection against cold-water disease in fish compared to inactivated whole cell *F. psychrophilum* bacterin. Contrary to Applicant's arguments the *F. psychrophilum* used in the study were cultured for 24 hours on modified cytophaga agar (MCY). The cultures were also transferred to fresh media after 24 hours which would minimize the accumulation of waste products etc., which trigger the bacteria to switch out of logarithmic growth phase (see page 170-bacterial strain and culture conditions on agar). Moreover, bacteria was scrapped from

MCY agar and used to inoculate medium, where cultures were grown and harvested by centrifugation while still in logarithmic growth phase (see page 173-culutre conditions in broth medium). Lastly, Rahman et al. disclose using said bacteria for a formalin-killed bacteria vaccine (page 170-preparation of vaccines). Absent evidence to the contrary, Rahman et al. disclose both the claimed method and composition.

With regard to Point 2, the Declaration under 37 C.F.R. §1.132 submitted on October 4, 2007 by Shun-Ichirou Oshima has been fully considered and deemed no-persuasive. The data disclosed in the declaration is not commensurate in scope with the data presented in Rahman et al. The data presented in the declaration does not use the exact parameters that were disclosed in the reference (see number 5 of the declaration). This is evidenced by Applicants submission that they started culturing with commonly used conditions, namely used cells from frozen stock of about 10^9 CFU/ml. This is further evidenced by the statement "proliferating potential of bacteria in each culture can be expected to be at the similar level since the culture conditions are quite similar to each other", indicating that while the cultures are similar they are not the same.

As previously presented, Rahman et al. disclose a *Flavobacterium psychrophilum* vaccine based on the antigenic outer membrane fraction of the cell (abstract). Rahman et al. disclose that the bacterin was inactivated with formalin (see page 170, preparation of the vaccines). Lastly, Rahman et al. disclose that the supernatant was centrifuged and re-suspended in distilled water (see page 171, 1st full paragraph). The vaccine of the prior art is the same of that which is claimed.

It should be remembered that the products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same or similar functional characteristics, i.e. the ability to prevent cold water disease in fish. The purification, isolation or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the process (i.e. isolation via centrifugation, filtration, or ultrasonic pulverization) does not change properties of the product in an unexpected manner. See *In re* Thorpe, 227 USPTO 964 (CAFC 1985); *In re* Marosi, 218 USPTO 289, 29222-293 (CAFC 1983); *In re* Brown, 173 USPTO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, great stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts to applicants product in order to overcome the aspect of the product's purity.

Moreover, Rahman et al. disclose a method for preventing cold-water disease in rainbow trout and ayu (abstract). Moreover, Rahman et al. disclose that the fish were immunized with a *Flavobacterium psychrophilum* vaccine based on the antigenic outer membrane fraction (see abstract and page 171-vaccination). The method of the prior art is the same of that which is claimed. Limitations such as an effective dosage range

and when to collect inactivated cells are being viewed as limitations of optimizing experimental parameters.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claims 3 and 19-24 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for the reasons of record. The cancellation of claims 4 and 25-30 renders the rejection of said claims moot.

Applicant argues that:

1) Applicants submit that the cancellation of claim 4 and the amendment to claim 2 to insert the term “and” in the place of "and/or" remedies this concern.

2) The present method claims relate to the protective immune response elicited by inactivated whole cells of *F. psychrophilum* in a logarithmic growth phase.

3) Examples 2 and 3 describe the preparation of the inactivated cells, while Examples 4 and 5 clearly show challenge experiments and the resulting protective immune response, which the Examiner alleges are not provided.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to a pharmaceutically administrable composition comprising inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture and at least one pharmaceutically acceptable carrier or adjuvant. Subsequent claims are drawn to a method for preventing the cold-water disease in fish, comprising administering an effective dosage of said composition to a fish in need thereof to thus prevent cold-water disease.

With regard to Point 1, Applicant is reminded that the primary purpose of this rejection was to demonstrate that Applicant's claims are broadly claimed and encompass administering an effective dosage of a pharmaceutical composition comprising components of inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase, wherein said components comprises cell membrane components, vesicles, and secretary products and at least one pharmaceutically acceptable carrier or adjuvant to a fish in need thereof to prevent cold-water disease. As well as administering an indistinguishable and undetermined number of cell membrane components, vesicles, and secretary products to prevent cold-water disease.

Therefore, contrary to Applicants arguments the specification has not demonstrated a method for preventing cold-water disease in fish, comprising administering inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase or components of inactivated cells of *Flavobacterium psychrophilum*, wherein said components comprises cell membrane components, vesicles, and secretary

products and at least one pharmaceutically acceptable carrier or adjuvant to a fish in need thereof to prevent cold-water disease.

With regard to Point 2, contrary to Applicant's arguments the rejected claims encompass whole cells as well as an unidentified amount of components from *Flavobacterium psychrophilum.* Moreover, the specification only demonstrates administering whole cells of NCMB1947 and 63724 to fish in need thereof. Consequently, the administration of said composition only increases the survival of the fish, which does not necessarily correlate to the prevention of cold-water disease in fish.

With regard to Point 3, Table 2 correlates to Examples 2-5, which relate to an increase in survival rate, average body weight and the number of deaths encountered. These parameters do not necessarily correlate to the protection of cold-water disease in fish. Additionally, the instant claims are not limited to inactivated whole cells of *Flavobacterium psychrophilum* and encompass both inactivated whole cells of *Flavobacterium psychrophilum* as well as components of *Flavobacterium psychrophilum*, which comprises cell membrane components, vesicles, and secretary products

As previously presented, to fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must demonstrate the ability to prevent cold-water disease in fish, so as to reasonably convey to the skilled artisan that Applicant has possession of the claimed invention.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to

practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Applicant was in possession of the claimed genus.

Moreover, the skilled artisan cannot envision administering an effective dosage of a pharmaceutical composition comprising components of a whole organism or inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at least one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products to a fish in need to prevent cold-water disease. The claims encompass a genus, which is not adequately described. Lastly, the instant claims are drawn to a method for the prevention of cold-water disease; however no protective (prevention) measures have been disclosed with inactivated whole cells, cell membrane components, vesicles, or secretary products of *Flavobacterium psychrophilum*. The specification is silent with regard to which component(s) will convey the protective response as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential ability to bind a specific biological agent. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

The University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an Applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC

§ 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention" (Id. at 1104). Moreover, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the Applicant had possession of the claimed invention at the time the instant application was filed.

6. The rejection of claims 3 and 19-24 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for the reasons of record. The cancellation of claims 4 and 25-30 renders the rejection of said claims moot.

Applicant argues that:

1) Applicants submit that the cancellation of claim 4 and the amendment to claim 2 to insert the term “and” in the place of "and/or" remedies this concern.

2) The present method claims relate to the protective immune response elicited by inactivated whole cells of *F. psychrophilum* in a logarithmic growth phase.

3) Examples 2 and 3 describe the preparation of the inactivated cells, while Examples 4 and 5 clearly show challenge experiments and the resulting protective immune response, which the Examiner alleges are not provided.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant invention is drawn to a pharmaceutically administrable composition comprising inactivated cells of *Flavobacterium psychrophilum* cultivated from a logarithmic growth phase culture and at least one pharmaceutically acceptable carrier or

adjuvant. Subsequent claims are drawn to a method for preventing the cold-water disease in fish, comprising administering an effective dosage of said composition to a fish in need thereof to thus prevent cold-water disease.

With regard to Point 1, Applicant is reminded that the primary purpose of this rejection was to demonstrate a lack of enablement. The enablement is based on a lack of proven efficacy as a vaccine. The specification has not demonstrated that administering an effective dosage of a pharmaceutical composition comprising components of inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase, wherein said components comprises cell membrane components, vesicles, and secretary products and at least one pharmaceutically acceptable carrier or adjuvant to a fish in need thereof will prevent cold-water disease. As well as administering an indistinguishable and undetermined number of cell membrane components, vesicles, and secretary products to prevent cold-water disease.

Therefore, contrary to Applicants arguments the specification has not demonstrated a method for preventing cold-water disease in fish, comprising administering inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase or components of inactivated cells of *Flavobacterium psychrophilum*, wherein said components comprises cell membrane components, vesicles, and secretary products and at least one pharmaceutically acceptable carrier or adjuvant to a fish in need thereof to prevent cold-water disease.

With regard to Point 2, contrary to Applicant's arguments the claims encompass whole cells as well as an unidentified amount of components from *Flavobacterium*

psychrophilum. Moreover, the specification only demonstrates administering whole cells of NCMB1947 and 63724 to fish in need thereof. Consequently, the administration of said composition only increases the survival of the fish, which does not necessarily correlate to the prevention of cold-water disease in fish.

With regard to Point 3, Table 2 correlates to Examples 2-5, which relate to an increase in survival rate, average body weight and the number of deaths encountered. These parameters do not necessarily correlate to the protection of cold-water disease in fish. Additionally, the instant claims are not limited to inactivated whole cells of *Flavobacterium psychrophilum* and encompass both inactivated whole cells of *Flavobacterium psychrophilum* as well as components of *Flavobacterium psychrophilum*, which comprises cell membrane components, vesicles, and secretary products

As previously presented, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the

invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CRFC1988). The Wands factors have been considered in the establishment of this scope of enablement rejection. These factors include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims are drawn to a method for preventing the cold-water disease in fish, comprising administering an effective dosage of a pharmaceutical composition comprising components of inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at least one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products to a fish in need thereof to thus prevent cold-water disease.

Breadth of the claims: The claims are broadly drawn and encompass administering an effective dosage of a pharmaceutical composition comprising components of inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and/or cell membrane components, vesicles, and/or secretary products and at least one pharmaceutically acceptable carrier or adjuvant to a fish in need thereof to prevent cold-water disease. Moreover, the instant claims encompass administering an indistinguishable and undetermined number of cell membrane components, vesicles, and/or secretary products to prevent cold-water disease. Lastly, the instant claims are drawn to a method for the prevention of cold-water disease; however no protective (prevention) measures have been disclosed.

Direction or guidance presented in the specification: To be a prophylactic method, said method must induce a protective immune response demonstrated by challenge experiments in an acceptable model. The specification does not provide substantive evidence that the claimed method is capable of inducing protective immunity against cold-water disease when administered a whole organism or inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at least one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products. The specification is equally silent with regard to which organism or cell components provide efficacy for the claimed method. Moreover, the components that convey the protective response have not been described. This demonstration is required for the skilled artisan to be able to use the claimed method for their intended purpose of preventing

cold-water disease in fish. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed composition, i.e. would not be able to accurately predict if protective immunity has been induced. The specification does not provide a demonstration where a pathogen free subject was administered the claimed composition and as a result the subject was protected from cold-water disease. There is insufficient direction or guidance presented in the specification with regard to the prevention of cold-water disease in a subject when said composition is administered.

Moreover, the specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. The specification does not demonstrate a method for preventing cold-water disease in fish, comprising administering an effective dosage of a pharmaceutical composition comprising a whole organism or components of inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at least one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products to a fish in need thereof to thus prevent cold-water disease. The specification generally discloses that administration of *Flavobacterium psychrophilum* G3724 increases the survival rate, but it does not contemplate administering said composition to demonstrate its efficacy against cold-water disease. Again, the specification does not provide a demonstration where a pathogen free subject or otherwise was administered inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at least one pharmaceutically

acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products and as a result the subjects disease was ameliorated or prevented. Increasing the subjects survival rater does not necessarily indicate that inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at lest one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products prevented the cold-water disease.

Presence or absence of working examples: There are no working examples, which suggest a method of preventing cold-water disease in fish when a fish is administered inactivated cells of *Flavobacterium psychrophilum* in a logarithmic growth phase and at lest one pharmaceutically acceptable carrier or adjuvant, wherein said components comprises cell membrane components, vesicles, and/or secretary products.

State of the prior art: Ryce et al. (Bacterial Coldwater Disease in Westslope Cutthroat Trout: Hatchery Epidemiology and Control, Montana Cooperative Fishery Research Unit; June 2004; pages 1-13) disclose that at present, the most effective form of disease control is to prevent outbreaks from occurring by reducing stress on the fish (see page 4, 1st paragraph).

Quantity of experimentation necessary: The quantity of experimentation necessary would be undue as no relevant evidence has been made of record establishing the amount of experimentation necessary. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot

be predicted from the disclosure how to make/use the claimed genus. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidence by the state of the prior art, attempting the construct and test variants of the claimed invention would constitute undue experimentation.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakia J. Tongue whose telephone number is 571-272-2921. The examiner can normally be reached on Monday-Friday 8-5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
12/17/07

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600